

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

- 1-26. (Cancelled)
27. (Withdrawn) A method comprising the steps:
- a) contacting a compound with a cell of claim 14 wherein the cell expresses a chimeric transcription factor;
  - b) measuring expression of a gene under promotional control of said transcription factor;
  - c) determining the effect of the compound on the amount of gene expression.
28. (Withdrawn) The method of claim 27 wherein the cell is modified to modulate the repressed state of the endogenous gene.
29. (Withdrawn) The method of claim 28 wherein the cell is modified by pre-exposure to drugs selected from a group consisting of: trichostatin A (TSA), and 5-aza-2'deoxyctidine (5-Aza-dC).
30. (Withdrawn) The method of claim 27 wherein step (b) measures the level of mRNA of the endogenous gene.
31. (Withdrawn) The method of claim 27 wherein step (b) measures the level of protein produced by the endogenous gene.
32. (Withdrawn) The method of claim 27 wherein the endogenous gene is an enzyme and step (b) is measured by monitoring the amount of enzyme activity of the endogenous gene.

33. (Withdrawn) The method of claim 33 wherein the endogenous gene is an enzyme selected from the group consisting of alkaline phosphatase, myeloperoxidase, and a serine protease.

34. (Withdrawn) The method of claim 27 wherein the induced endogenous gene produces a cell surface protein.

35. (Withdrawn) The method of claim 34 wherein the cells surface protein is selected from the group consisting of a CD antigen, a non-CD antigen transmembrane protein, and placental alkaline phosphatase.

36. (Withdrawn) The method of claim 27 wherein the cells are lysed and the product of the induction of the endogenous gene is measured in the cell lysate.

37. (Withdrawn) The method of claim 27 wherein the induction of the endogenous gene results in a change in cellular phenotype that is measured in step (b).

38. (Withdrawn) The method of claim 37 wherein the cellular phenotype is translocation of a protein from one cellular component to a different cellular component.

39. (Withdrawn) A method comprising the steps:  
a) contacting a compound, an extracellular ligand and a cell of claim 14, said cell being capable of responding to said ligand and containing a chimeric transcription factor;  
b) measuring expression of an endogenous gene under transcription control of said exogenous transcription factor; and  
c) determining the effect of the compound on the amount of gene expression.

40. (Withdrawn) The method of claim 39 wherein the cell is modified to modulate the repressed state of the endogenous gene.

41. (Withdrawn) The method of claim 40 wherein the cell is modified by pre-exposure to drugs selected from a group consisting of: trichostatin A (TSA), and 5-aza-2'deoxyctidine (5-Aza-dC).

42. (Withdrawn) The method of claim 39 wherein step (b) measures the level of mRNA of the endogenous gene.

43. (Withdrawn) The method of claim 39 wherein step (b) measures the level of protein produced by the endogenous gene.

44. (Withdrawn) The method of claim 39 wherein the endogenous gene is an enzyme and step (b) is measured by monitoring the amount of enzyme activity of the endogenous gene.

45. (Withdrawn) The method of claim 44 wherein the endogenous gene is an enzyme selected from the group consisting of alkaline phosphatase, myeloperoxidase, and a serine protease.

46. (Withdrawn) The method of claim 39 wherein the induced endogenous gene produces a cell surface protein.

47. (Withdrawn) The method of claim 46 wherein the cells surface protein is selected from the group consisting of a CD antigen, a non-CD antigen transmembrane protein, and placental alkaline phosphatase.

48. (Withdrawn) The method of claim 39 wherein the cells are lysed and the product of the induction of the endogenous gene is measured in the cell lysate.

49. (Withdrawn) The method of claim 39 wherein the induction of the endogenous gene results in a change in cellular phenotype that is measured in step (b).

50. (Withdrawn) The method of claim 49 wherein the cellular phenotype is translocation of a protein from one cellular component to a different cellular component.

51-65. (Cancelled)

66. (Withdrawn) A method to modulate the amount of a receptor comprising the steps:

- a) providing a cell of claim 53 wherein the cell contains an inducible transcription factor that up-regulates a receptor of interest in the cell; and
  - b) stimulating the function of the transcription factor with an extracellular ligand such that the receptor is produced by the cell
- wherein the amount the receptor is modulated by the activity of the transcription factor.

67. (Withdrawn) A method comprising the steps:

- a) contacting a compound with an un-stimulated cell of claim 53 and contacting a compound with a stimulated cell of claim 53 such that the stimulated cell expresses a receptor;
- b) measuring the activity of the receptor in the un-stimulated cell and the stimulated cell; and
- c) determining the effect of the compound on the activity of the receptor.

68. (Withdrawn) A method comprising the steps:

- a) contacting a compound and an extracellular ligand with an unstimulated cell of claim 53 and contacting a compound and an extracellular ligand with a stimulated cell of claim 53 such that the stimulated cell expresses a receptor;
- b) measuring the activity of the receptor in the unstimulated cell and the stimulated cell; and
- c) determining the effect of the compound on the activity of the receptor.

69-71. (Cancelled)

72. (Withdrawn) A method comprising the steps:

- a) contacting a compound with a cell of claim 71, said cell containing a membrane bound, constitutively active transcription factor;
- b) stimulating activity of a protease by the compound to release the transcription factor from the membrane and therefore allowing the transcription factor to translocate to the nucleus;
- c) measuring expression of a gene under promotional control of the membrane bound transcription factor; and
- d) determining the effect of the compound on the amount of gene expression.

73. (Withdrawn) A method comprising the steps:

- a) contacting a compound and an extracellular ligand with a cell of claim 71, said cell containing a membrane bound, constitutively active transcription factor;
- b) stimulating activity of a protease by either the compound or the ligand to release the transcription factor from the membrane and therefore allowing the transcription factor to translocate to the nucleus;
- c) measuring expression of a gene under promotional control of the membrane bound transcription factor; and
- d) determining the effect of the compound on the amount of gene expression.

74. (Withdrawn) A compound discovered using the method of claim 27.

75. (Withdrawn) A pharmaceutical composition comprising a compound of claim 74.

76. (Withdrawn) A compound discovered using the method of claim 39.

77. (Withdrawn) A pharmaceutical composition comprising a compound of claim 76.

78. (Withdrawn) A compound discovered using the method of claim 67.

79. (Withdrawn) A pharmaceutical composition comprising a compound of claim 78.

80. (Withdrawn) A compound discovered using the method of claim 68.

81. (Withdrawn) A pharmaceutical composition comprising a compound of claim 81.

82. (Currently Amended) A compound that modulates the response of an ~~extracellular ligand~~ a cellular receptor by binding to the receptor; the compound identified by a method comprising the steps of:

a) contacting a compound suspected of being ~~a compound that modulates~~ modulator of the response of ~~an extracellular ligand~~ a cellular receptor by binding thereto with a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:

- i) a constitutively active domain;
- ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and
- iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably linked to the

DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease activated as a result of a signal transduced upon the binding of the compound to the receptor, by the compound to the protease activity releasing the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; and

c) measuring expression of a gene under promotional control of the released membrane-bound transcription factor[.]; and whereby an increase or decrease in expression of the gene is indicative that the compound modulates the response of an extracellular ligandreceptor.

d) comparing the expression to that of a control assay without the compound whereby an increase or decrease in expression of the gene is indicative that the compound modulates the response of the cellular receptor.

83. (Previously Presented) A pharmaceutical composition comprising a compound of claim 82.

84. (Currently Amended) A compound that modulates the response of an extracellular ligand a cellular receptor to the binding of an extracellular ligand thereto; the compound identified by a method comprising the steps of:

a) contacting a compound suspected of being a compound that modulates the response of an extracellular ligand the cellular receptor to the binding of an extracellular ligand thereto with an extracellular ligand and a cell having a nucleus and containing a

membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:

- i) a constitutively active domain;
- ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and
- iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease ~~by~~ as a result of a signal transduced upon the binding of either the compound or the ligand to the receptor, the protease activity releasing to release the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; ~~and~~

c) measuring expression of a gene under promotional control of the membrane-bound transcription factor[.]; and ~~whereby an increase or decrease in expression of the gene is indicative that the compound modulates the response of an extracellular ligand~~

d) comparing the expression to that of a control assay without the compound, whereby an increase or decrease in expression of the gene is indicative that the compound modulates the response of the cellular receptor to the binding of an extracellular ligand.

85. (Previously Presented) A pharmaceutical composition comprising a compound of claim 84.



86. (New) A method for identifying a compound that modulates the response of a cellular receptor to the binding of an extracellular ligand thereto, the method comprising the steps of:

a) contacting a compound suspected of being a modulator of the response of the cellular receptor to binding of an extracellular ligand with a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:

- i) a constitutively active domain;
- ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and
- iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease activated as a result of a signal transduced upon the binding of the compound to the receptor, the protease activity releasing the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus;

c) measuring expression of a gene under promotional control of the released membrane-bound transcription factor; and

d) comparing the expression to that of a control assay without the compound, whereby an increase or decrease in expression of the gene is indicative that the compound modulates the response of the cellular receptor to binding of an extracellular ligand thereto.